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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/986,750	11/09/2001	Richard M. Pires	0942.5080001/RWE/FRC	5957
26111	7590	06/24/2004	EXAMINER	
STERNE, KESSLER, GOLDSTEIN & FOX PLLC 1100 NEW YORK AVENUE, N.W. WASHINGTON, DC 20005			SCHULTZ, JAMES	
			ART UNIT	PAPER NUMBER
			1635	

DATE MAILED: 06/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/986,750

Applicant(s)

PIRES ET AL.

Examiner

J. Douglas Schultz, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 08 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-9 and 11-25 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948)                                    | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Status of Application/Amendment/Claims***

1. Applicant's response filed April 8, 2004 has been considered. Rejections and/or objections not reiterated from the previous office action mailed March 11, 2003 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Specification***

3. The specification is objected to because the lone example refers to the chromatographic outputs depicted at figure 5A and 5B, when said figure actually refers solely to a diagram of oligonucleotide synthesis. Figure 6 contains HPLC results, and is referred to later in the example; if it is applicants intent to refer to the chromatograph of figure 6A and 6B, amendment to that effect would obviate this objection. Otherwise, clarification is required.

### ***Response to Arguments, Claim Rejections - 35 USC § 103***

4. Claims 1-9, 11-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kempe et al., in view of Lyttle et al. for the same reasons of record as set forth in the Office action mailed July 2, 2002.

Applicants traverse the rejection by arguing that Lyttle, who teaches a method of synthesizing oligonucleotides using universal linkers that are cleaved with aqueous ammonium

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hydroxide, teaches away from its combination with Kempe, who teaches using a linker cleaved with gaseous ammonium hydroxide. Applicants argue that “Lyttle teaches that reagents harsher than aqueous ammonium hydroxide, e.g. gaseous ammonia, are a limitation in the removal process, which should be avoided.”

These arguments are not considered convincing. In fact, the quotation provided by Applicants in support of their conclusion that Lyttle actually teaches away, when viewed in its proper context, simply explains why a different linker has not been widely adopted for use, and further, provides a context for why the new linkers of Lyttle et al. are a contribution to the art. In other words, Applicants’ quoted phrase explains why the findings of Lyttle et al. are novel and thus worthy of publication. As such, this quote, taken out of context, does not properly constitute an example of teaching away.

Lyttle never indicates that harsher reagents are to be avoided when using the linkers newly set forth therein. Lyttle is not considered to teach away merely because he suggests that strongly basic conditions were required to cleave universal linkers that existed prior to the disclosure of Lyttle. In fact, Lyttle clearly indicates his opinion that the linkers newly described in the manuscript represent an advance over the older universal linkers; “our new formulation of the vicinal diol universal support offers several advantages besides the added convenience of using a single support material for every sequence. 3’-Linker cleavage times are shorter than with other vicinal diol universal supports at the same temperature and conditions (16 h)<sup>5</sup>. Most importantly, DNA products made with these new materials are free of 3’- modified contaminants... Additionally, no non-volatile salts or other reagents besides aqueous ammonia are needed for deprotection and cleavage, so the crude DNA can be used for a number of

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applications without the necessity of post-synthetic desalting steps..." Thus it is maintained that Lyttle *et al.* believes the newly created linkers therein to be superior to those previously known in the art, and importantly, never teaches or suggests that they are contraindicated by the presence of a stronger reagent. Lyttle *et al.* therefore does not teach away.

Applicants further argue that no motivation exists to use the universal linkers of Lyttle in the method of cleavage using gaseous ammonia, because Lyttle teaches that mild reagents such as aqueous ammonium hydroxide are sufficient for removal, and that accordingly one would not have been motivated to experiment with harsher reagents, such as gaseous ammonia. This is not considered convincing, because Kempe clearly teaches that the method of cleaving oligos using gaseous ammonia is faster and requires fewer constituents, thus leading to easier methods purification. The ability to perform methods faster and simpler is considered substantial motivation. Since nothing about these methods indicates that gaseous ammonia wouldn't work in combination with the linkers of Lyttle, and because one of ordinary skill would be motivated to combine the faster cleavage methods of Kempe with the universal linkers of Lyttle, the rejection is maintained.

### ***Claim Rejections - 35 USC § 102***

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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Claims 1, 11-15 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Kempe (of record).

The instant claims are drawn to a method for cleavage of a linker from an oligonucleotide comprising contacting a conjugate comprising an oligonucleotide, a linker, and a solid support with gaseous ammonia vapors under conditions that result in the cleavage of the linker from the oligonucleotide, wherein the method is carried out from 1 to 240 minutes, or 60 minutes, or wherein the temperature of the method is carried out at from 24<sup>0</sup> to 150<sup>0</sup> C, or at about 95<sup>0</sup> C.

Kempe teaches a method for cleavage of a linker from an oligonucleotide comprising contacting a conjugate comprising an oligonucleotide, a linker arm (col. 1), and a solid support with gaseous ammonia vapors under conditions that result in the cleavage of the linker from the oligonucleotide, wherein the method is carried out from 1 to 240 minutes, or 60 minutes (col. 4 line 10), or wherein the temperature of the method is carried out at from room temperature to 150<sup>0</sup> C, or at about 95<sup>0</sup> C (col. 8, lines 1-5).

### ***Conclusion***

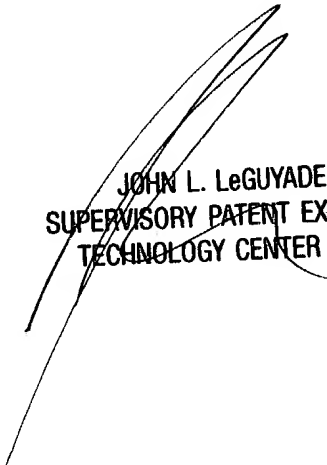
6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Douglas Schultz, Ph.D. whose telephone number is 571-272-0763. The examiner can normally be reached on 8:00-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JD Schultz, PhD

  
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